

Please add new claims 54 -56 as follows:

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Sub F 54
(New) An isolated FADD polypeptide fragment of the protein of claim 1, wherein the fragment has the ability to bind the cytoplasmic domain of the Fas receptor.

55. (New) An isolated FADD polypeptide fragment of the protein of claim 1, wherein the fragment has the ability to induce apoptosis in a suitable cell.

56. (New) An isolated FADD protein or fragment thereof of any claims 1, 54 or 55, which has been recombinantly produced *in vitro* and isolated from a cell.

II. REMARKS

Claims 1-6, 21, 23, 24, 29-32 and 37 to 53 are pending in this application. Claim 53 has been withdrawn from consideration by the Office pursuant to an election/restriction requirement. Claims 1-6, 21, 23, 24, 29-32 and 37-52 stand variously rejected under 35 U.S.C. §§ 112, 102 and 103.

Claims 6, 24, 31-35, 44, 47, and 50-52 have been canceled without prejudice to Applicants' right to pursue the same or similar claims in a continuation application. The cancellation of these claims, and the amendments to the claims made herein are not intended to be a dedication to the public of the subject matter of the claims as previously presented.

Claims 1-5, 21, 29, 30, 37-43 and 45-49, have been amended herein. New claims 54-56 have been added. Support for the amendments to the claims and the addition of new claims 54-56 can be found throughout the specification, for example in the sequence identification listings, and on pages 14 and 15 which describe the fragments and functions of the claimed proteins and fragments. These amendments do not introduce new matter and have been made in a sincere effort to place the pending application in condition for allowance. The amendments were not made earlier since it was Applicants' position that the claims as previously presented defined

patentable subject matter. Entry of these amendments and allowance of the application is respectfully requested.

Election/Restriction

Claim 53 is alleged to be directed to an invention that is independent and distinct from the invention originally claimed. In support of this election requirement, the Examiner states:

The method of claim 53 and the methods of claims 29 and 30 are independent and distinct, wherein each method performs different functions, using different starting materials and/or process steps.

Furthermore, the product of claims 1-6, 21, 23, 24, 31, 32 and 37-52 and the method of claim 53 are related as product and process of use. ... In the instant case the product can be used in an immunization protocol for the production of antibodies."

Applicants traverse and request rejoinder of claim 53 and its dependent claims (2, 6, 21, 23, 24- and 46-52). Claim 53 is directed to a process for purifying a FADD protein, essentially by binding it to the cytoplasmic domain of the Fas receptor and isolating the FADD-Fas complex. Pursuant to the Rules of Rejoinder (See, e.g., M.P.E.P § 821.04), an applicant may present claims directed to the process of making and/or using the patentable product by way of amendment. These process claims will be entered as matter of right if the amendment is presented prior to final rejection or allowance. In the pending case, claim 53 should be entered and considered because it is one way to purify the proteins of claims 1 and its dependents. The product by process of claims 2, 21, 23, 24 and 46-49, and the product claims of claim 1 and its dependents, each can be used for immunization protocols. Reconsideration and withdrawal of this ground for objection to claim 53 and its dependents is respectfully requested.

Formal Matters

Applicants note the change in Group Art Unit and thank the Examiner for withdrawal of the objections to claim 23 and to the Disclosure.

Claims 2, 6, 21, 23, 24 and 46-52 are objected to because they depend from allegedly distinct claim 53. Claims 6 and 50-52 have been canceled without prejudice or disclaimer. For

the reasons provided above, claims 2, 21, 23, 24 and 46-49, should be examined with claim 53. Reconsideration and entry of claims 2, 6, 21, 23, 24 and 46-52, is respectfully requested.

Objection to the Drawings

Applicants note that this is a reiteration of the informality raised in the previous Office Action (Paper # 16). In Applicants' prior response, new figures were submitted and the specification was amended accordingly. In the event the Office did not receive the substitute figures previously submitted by Applicants, an additional copy is submitted herewith. In view of the filing of these substitute drawings and the amendments previously requested and entered, reconsideration and withdrawal of the objection is respectfully requested.

35 U.S.C. § 112, First Paragraph

Written Description Issues

The rejection as applied to claims 1 and 3-5, has been withdrawn. The Office maintained the rejection for claims 2, 6, 21, 23, 24 and 29-32. Newly added claims 44 and 46-52 were newly rejected. Applicants traverse each rejection for the reasons discussed below.

Claims 3, 6, 21, 23 and 47-49 stand rejected because there is allegedly no support for the recitation of "amino acids 24 to 208." Applicants direct the Examiner's attention to SEQ ID NO:1, feature (ix) nucleic acids 198-753; Figure 2; and page 44, line 10 which indicate that amino acids 24 to 208 correspond to originally disclosed clone 15.

With regard to claim 41, Applicants have corrected the typographical error and amended the claim to recite "amino acids 41 to 208." Support for this amendment is found on page 15, lines 8-16 and in SEQ ID NO:1 feature (ix) which describe a C-terminal fragment of the FADD protein.

Claim 44 has been canceled without prejudice or disclaimer, thereby removing this ground for rejection.

Claim 45 finds support on page 4, line 4; Figure 2B; and page 9, lines 1-15 which describe how, in the FADD mutant in which amino acid residue 121 is altered, the remaining

amino acid residues (*i.e.* 1-120 and 122-208) can contain conservative substitutions. The claim also has been amended to correct a typographical error. Residue "123" now recites "122."

Finally, it is alleged that the recitation of "stabilizer" and "preservative" in claims 49 and 51 is not supported by the specification as filed. Claim 51 has been canceled without prejudice or disclaimer. For claim 49, Applicants direct the Examiner's attention to page 10, lines 21 to 24, where these terms are defined and where Applicants refer to Remington's Pharmaceutical Manual for further disclosure of suitable stabilizers and preservatives.

In view of the foregoing, withdrawal of the rejections under 35 U.S.C. § 112, first paragraph written description is respectfully requested.

Enablement Issues

The Office removed the rejection of claims 3-5 under 35 U.S.C. § 112, first paragraph (enablement) but maintained it for claim 32. The Office opined that without recited structure, the claim lacks enablement.

Applicants traverse. Claim 32 is enabled because the specification teaches one of skill in the art how to make and use the invention of the claim, *i.e.*, FADD fragments. The specification provides several means to make FADD (chemically, recombinantly or to purify). How to make these fragments of FADD also is taught. Therefore, the specification as filed enables the claim. The rejection should therefore be withdrawn.

Claims 29 and 30 remain rejected under 35 U.S.C. § 112, first paragraph. Without conceding the correctness of the Examiner's position and merely to expedite examination, claims 29 and 30 have been amended in a sincere effort to place the claims in condition for allowance. Removal of this rejection is respectfully requested.

Claims 1-6, 21, 23, 24, and 29-32 and 37-52, are newly rejected under 35 U.S.C. § 112, first paragraph because the claims allegedly encompass FADD polypeptides with an unlimited number of conservative amino acid substitutions. The Examiner postulated that the effects of mutations may be cumulative, and therefore, the FADD proteins may only be able to tolerate a limited number of amino acid substitutions and retain their functional activity. Without

conceding the correctness of the Office's position, and merely to expedite examination, the independent claims have been amended in accordance with the Office's suggestions.

35 U.S.C. § 112, Second Paragraph

Applicants acknowledge withdrawal of the rejection of claims 21 and 23. Claims 2, 31, 32, 37-44, 49 and 51 stand rejected under 35 U.S.C. § 112, second paragraph as allegedly vague and indefinite.

Claim 31 and 32 are alleged to be unclear in not reciting the nature of the claimed protein. The Office remarked that the claims are unclear on the ground that all DNA are recombinant and that all proteins are the result of recombination.

Applicants direct the Office's attention to page 16, line 28 to page 17, line 29 of the specification which defines and illustrates how "recombinant" proteins can be produced.

Applicants' use of the term is in accordance with its generally accepted usage. See, for example, page 269 of King and Stanfield, eds. A DICTIONARY OF GENETICS, FOURTH EDITION, Oxford University Press (1990), wherein it defines recombinant DNA as "a composite DNA molecule created *in vitro* by joining a foreign DNA with a vector molecule." (Copy enclosed). Thus, one of skill in the art would understand that a protein that is not naturally occurring is one which is not purified from *in vivo* sources. Reconsideration and withdrawal of the rejection is respectfully requested.

Claims 37-43 are also alleged to be indefinite because they do not recite where the claimed fragment is obtained. Applicants have amended these claims to recite "a polypeptide fragment of the protein of claim 1," thereby obviating this rejection.

Claims 44 and 51 have been canceled without prejudice or disclaimer, thereby removing this ground for rejection.

Finally, claims 49 has been amended to specify that the carrier is not a "detectable label". Support for this amendment can be found, for example, on page 18, lines 10-26.

Applicants have addressed all remaining issues under 35 U.S.C. § 112, second paragraph and respectfully submit that withdrawal of these rejections is in order.

35 U.S.C. § 102(b)

Claims 2, 6, 21, 23, 24, 31, 32 and 46-49 rejected over Itoh. In particular, it is maintained that, absent structural limitations in the claims, Itoh discloses the claimed FADD protein. By amendment herein, claims 2, 21, 23, 24 and 46-49 now recite certain structural limitations which distinguish the claimed protein from that disclosed in Itoh. Claims 6, 24, 31 and 32 have been canceled without prejudice or disclaimer. Claim 2, now recites that the purified protein have an apparent molecular weight of about 23.3 kDa as determined by an SDS polyacrylamide gel under reducing conditions. Although Itoh does not provide a molecular weight for the Fas antigen, it does recite that the fas antigen consists of 325 amino acids. The Fas antigen is significantly larger than the 208 amino acid FADD protein of this invention. Therefore, the Fas antigen is not encompassed by the language of claim 2. Therefore, withdrawal of this rejection is respectfully requested.

35 U.S.C. § 103

Claims 21 and 23 stand rejected over Itoh in view of Berg, and claims 2 and 46 stand rejected over Itoh in view of Berg and in further view of Sambrook. Claims 6 and 52 also stand rejected over Itoh in view of Sambrook. The primary reference, Itoh is cited, as above, as disclosing a recombinantly produced and isolated Fas receptor that allegedly meets the structural and functional definition of a FADD protein. Berg is cited for disclosing a process for chemical synthesis of proteins. Sambrook is cited for disclosing general techniques regarding recombinant production of proteins in bacteria. It is alleged that it would have been obvious to one skilled in the art to arrive at the claimed compositions in view of the cited references.

The currently pending, rejected claims have been amended to specify certain structural and functional limitations of the FADD protein. As a result, the primary reference does not teach or suggest the claimed products. Furthermore, no combination of the cited references would result in these products. Accordingly, Applicants respectfully request that the rejections under 35 U.S.C. § 103 be withdrawn.

III. CONCLUSION

If a telephonic interview would be of assistance in advancing prosecution of this application, the Examiner is invited to telephone the undersigned attorney at the number listed below.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, Applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 203442107020. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

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